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Search	Most Recent Queries	Time	Result
<u>#26</u>	Search EphA2 and peptide and HLA	07:16:08	<u>4</u>
<u>#33</u>	Search eck and peptide and HLA	07:13:54	<u>3</u>
<u>#24</u>	Search eck and peptide	07:13:50	<u>142</u>
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<u>#29</u>	Search ephrin	07:12:41	<u>1102</u>
<u>#22</u>	Search ephrin and epitope	07:12:33	<u>4</u>
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<u>#25</u>	Search EphA2 and peptide	07:09:44	<u>97</u>
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<u>#19</u>	Search Eph and epitope	07:04:21	<u>6</u>
<u>#18</u>	Search Eph and "T epitope"	07:04:00	<u>0</u>
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<u>#14</u>	Search vonderheide RH and HLA and anderson	06:58:33	<u>6</u>
<u>#13</u>	Search vonderheide RH and HLA	06:57:55	<u>16</u>
<u>#12</u>	Search vonderheide RH	06:57:48	<u>49</u>
<u>#1</u>	Search "reverse immunology"	06:30:46	<u>34</u>
<u>#4</u>	Search "reverse immunology" and kinase	06:27:50	<u>6</u>
<u>#3</u>	Search "reverse immunology" and Eck	06:27:26	<u>1</u>
<u>#2</u>	Search "reverse immunology" and EphA2	06:27:05	<u>1</u>

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ephrin and HLA and peptide and "t cell" and "t lymphocyte"

PAT. NO.	Title
1 <a href="#">7,229,760</a>	<b>T</b> <a href="#">mRNA amplification</a>
2 <a href="#">7,189,507</a>	<b>T</b> <a href="#">Methods of diagnosis of ovarian cancer, compositions and methods of screening for modulators of ovarian cancer</a>
3 <a href="#">6,974,667</a>	<b>T</b> <a href="#">Gene expression profiles in liver cancer</a>
4 <a href="#">6,964,868</a>	<b>T</b> <a href="#">Human genes and gene expression products II</a>
5 <a href="#">6,943,241</a>	<b>T</b> <a href="#">Full-length cDNA</a>
6 <a href="#">6,905,874</a>	<b>T</b> <a href="#">Simultaneous stimulation and concentration of cells</a>
7 <a href="#">6,900,016</a>	<b>T</b> <a href="#">Polymorphisms in known genes associated with inflammatory autoimmune disease, methods of detection and uses thereof</a>
8 <a href="#">6,867,041</a>	<b>T</b> <a href="#">Simultaneous stimulation and concentration of cells</a>
9 <a href="#">6,797,514</a>	<b>T</b> <a href="#">Simultaneous stimulation and concentration of cells</a>
10 <a href="#">6,783,969</a>	<b>T</b> <a href="#">Cathepsin V-like polypeptides</a>
11 <a href="#">6,706,867</a>	<b>T</b> <a href="#">DNA array sequence selection</a>
12 <a href="#">6,670,464</a>	<b>T</b> <a href="#">Nucleic acids containing single nucleotide polymorphisms and methods of use thereof</a>

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epha2 and HLA and epitope and peptide and "T cell" and "T lymphocyte": 18 applications.

Hits 1 through 18 out of 18

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[Refine Search](#) epha2 and HLA and epitope and peptide and "T cell" and "T lymphocyte"

PUB. APP. NO.	Title
1 <a href="#">20070224188</a>	<a href="#">Variant Fc Regions</a>
2 <a href="#">20070220620</a>	<a href="#">TAT-046 and methods of assessing and treating cancer</a>
3 <a href="#">20070192887</a>	<a href="#">TAT-042 and methods of assessing and treating cancer</a>
4 <a href="#">20070192886</a>	<a href="#">TAT-044 and methods of assessing and treating cancer</a>
5 <a href="#">20070192885</a>	<a href="#">TAT-039 and methods of assessing and treating cancer</a>
6 <a href="#">20070192884</a>	<a href="#">TAT-038 and methods of assessing and treating cancer</a>
7 <a href="#">20070192883</a>	<a href="#">TAT-028 and methods of assessing and treating cancer</a>
8 <a href="#">20070186295</a>	<a href="#">TAT-036 and methods of assessing and treating cancer</a>
9 <a href="#">20070186294</a>	<a href="#">TAT-030 and methods of assessing and treating cancer</a>
10 <a href="#">20070180545</a>	<a href="#">TAT-031 and methods of assessing and treating cancer</a>
11 <a href="#">20070167375</a>	<a href="#">Peptide analogs capable of enhancing stimulation of a glioma-specific CTL response</a>
12 <a href="#">20070111260</a>	<a href="#">Cell display of antibody libraries</a>
13 <a href="#">20070106065</a>	<a href="#">TAT- 001 and methods of assessing and treating cancer</a>
14 <a href="#">20060019899</a>	<a href="#">EphA2 T-cell epitopes and uses therefor</a>
15 <a href="#">20050123596</a>	<a href="#">pH-triggered microparticles</a>
16 <a href="#">20050048550</a>	<a href="#">EphA2 T-cell epitope agonists and uses therefor</a>
17 <a href="#">20040197343</a>	<a href="#">Modified free-living microbes, vaccine compositions and methods of use thereof</a>
18 <a href="#">20030194696</a>	<a href="#">Methods of producing a library and methods of selecting polynucleotides of interest</a>

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**Results of Search in US Patent Collection db for:****((Epha2 AND HLA) AND peptide) AND vaccine): 2 patents.****Hits 1 through 2 out of 2**[Jump To](#)[Refine Search](#)PAT.  
NO.

Title

- 1 7,189,507 **T** Methods of diagnosis of ovarian cancer, compositions and methods of screening for modulators of ovarian cancer
- 2 6,706,867 **T** DNA array sequence selection
- 

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\*\*\*File 156, ToxFile

\*\*\*Files 154 &amp; 155, MEDLINE

\*\*\*File 5, BIOSIS Previews - archival data added

\*\*\*Files 340, 341 &amp; 942, CLAIMS/U.S. Patents - 2006 reload now online

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**NEWS**

Chemical Structure Searching now available in Prous Science Drug Data Report (F452), Prous Science Drugs of the Future (F453), IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus (File 302).

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\$0.95 Estimated cost File1

\$0.53 INTERNET

\$1.48 Estimated cost this search

\$1.48 Estimated total session cost 0.272 DialUnits

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File 159:Cancerlit 1975-2002/Oct

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Set	Items	Description
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?

S (EPHA2 OR ECK OR EPHRIN)

796	EPHA2
1204	ECK
4740	EPHRIN

S1 6271 (EPHA2 OR ECK OR EPHRIN)

?

S S1 AND (HLA AND PEPTIDE)

6271	S1
326070	HLA
1235328	PEPTIDE

S2 16 S1 AND (HLA AND PEPTIDE)

?

S S2 AND (EPITOPE)

16	S2
161858	EPITOPE

S3 13 S2 AND (EPITOPE)

?

S S3 AND (T (N) (CELL OR LYMPHOCYTE))

Processing

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Completed processing all files

13	S3
3724330	T
12027283	CELL
936122	LYMPHOCYTE
975167	T(N)(CELL OR LYMPHOCYTE)

S4 10 S3 AND (T (N) (CELL OR LYMPHOCYTE))

?

TYPE S4/FULL/1-10

4/9/1 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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15740128 PMID: 16207473

**EphA2 as a glioma-associated antigen: a novel target for glioma vaccines.**

Hatano Manabu; Eguchi Junichi; Tatsumi Tomohide; Kuwashima Naruo; Dusak Jill E; Kinch Michel S; Pollack Ian F; Hamilton Ronald L; Storkus Walter J; Okada Hideho

Department of Neurological Surgery, University of Pittsburgh School of Medicine and University of Pittsburgh Cancer Institute, Pittsburgh, PA 15213, USA.

Neoplasia (New York, N.Y.) (United States) Aug 2005, 7 (8) p717-22, ISSN 1522-8002--Print Journal Code: 100886622

Contract/Grant No.: P01 NS40923; NS; NINDS

Publishing Model Print

Document type: Journal Article; Research Support, N.I.H., Extramural; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

EphA2 is a receptor tyrosine kinase and is frequently overexpressed in a wide array of advanced cancers. We demonstrate in the current study that the EphA2 protein is restrictedly expressed in primary glioblastoma multiforme and anaplastic astrocytoma tissues in comparison to normal brain tissues. To evaluate the possibility of targeting EphA2 in glioma vaccine strategies, we stimulated human leukocyte antigen (HLA) A2+ peripheral blood mononuclear cells (PBMCs) obtained from healthy donors and glioma patients with autologous dendritic cells (DCs) loaded with synthetic EphA2883-891 peptide (TLADFDPV), which has previously been reported to induce interferon-gamma in HLA-A2+ PBMCs. Stimulated PBMCs demonstrated antigen-specific cytotoxic T lymphocyte (CTL) responses as detected by specific lysis of T2 cells loaded with the EphA2883 peptide as well as HLA-A2+ glioma cells, SNB19 and U251, that express EphA2. Furthermore, in vivo immunization of HLA-A2 transgenic HHD mice with the EphA2883-891 peptide resulted in the development of an epitope-specific CTL response in splenocytes, despite the fact that EphA2883-891 is an autoantigen in these mice. Taken together, these data suggest that EphA2883-891 may be an attractive antigen epitope for molecularly targeted glioma vaccines.

Descriptors: \*Antigens, Neoplasm--biosynthesis--BI; \*Brain Neoplasms--immunology--IM; \*Cancer Vaccines--pharmacology--PD; \*Glioblastoma--immunology--IM; \*Receptor, EphA2--biosynthesis--BI; Animals; Antigens, Neoplasm--immunology--IM; Brain Neoplasms--metabolism--ME; Cell Line, Tumor; Glioblastoma--metabolism--ME; HLA-A2 Antigen--immunology--IM; Humans; Leukocytes, Mononuclear--immunology--IM; Mice; Mice, Transgenic; Receptor, EphA2--administration and dosage--AD; Receptor, EphA2--immunology--IM; Spleen--cytology--CY; Spleen--drug effects--DE; Spleen--immunology--IM; T-Lymphocytes, Cytotoxic--immunology--IM

CAS Registry No.: 0 (Antigens, Neoplasm); 0 (Cancer Vaccines); 0 (HLA-A2 Antigen)

Enzyme No.: EC 2.7.1.112 (Receptor, EphA2)

Record Date Created: 20051006

Record Date Completed: 20051223

4/9/2 (Item 2 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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14639580 PMID: 14679012

**EphA2 as target of anticancer immunotherapy: identification of HLA-A\*0201-restricted epitopes.**

Alves Pedro M S; Faure Olivier; Graff-Dubois Stephanie; Gross David-Alexandre; Cornet Sebastien; Chouaib Salem; Miconnet Isabelle; Lemonnier Francois A; Kosmatopoulos Kostas

INSERM487, Institut Gustave Roussy, Villejuif. Unite d'Immunité Cellulaire Antivirale, Institut Pasteur, Paris. Immuno-Designed Molecules, Paris, France.

Cancer research (United States) Dec 1 2003, 63 (23) p8476-80, ISSN 0008-5472--Print Journal Code: 2984705R

Publishing Model Print

Document type: Journal Article; Research Support, Non-U.S. Gov't

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

EphA2 (Eck) is a tyrosine kinase receptor that is overexpressed in several human cancers such as breast, colon, lung, prostate, gastric carcinoma, and metastatic melanoma but not in nonmalignant counterparts. To validate EphA2 as a tumor antigen recognized by CD8+ T lymphocytes, we used reverse immunology approach to identify HLA-A\*0201-restricted epitopes. Peptides bearing the HLA-A\*0201-specific anchor motifs were analyzed for their capacity to bind and stabilize the HLA-A\*0201 molecules. Two peptides, EphA2(58) and EphA2(550), with a high affinity for HLA-A\*0201 were selected. Both peptides were immunogenic in the HLA-A\*0201-transgenic HHD mice. Interestingly, peptide-specific murine CTLs cell lines responded to COS-7 cells coexpressing HLA-A\*0201 and EphA2 and to EphA2-positive human tumor cells of various origin (renal cell, lung, and colon carcinoma and sarcoma). This demonstrates that EphA2(58) and EphA2(550) are naturally processed from endogenous EphA2. In addition, EphA2(58) and EphA2(550) stimulated specific CD8(+) T cells from healthy donor peripheral blood mononuclear cells. These T cells recognized EphA2-positive human tumor cells in an HLA-A\*0201-restricted manner. Interestingly, EphA2-specific CD8+ T cells were detected in the peripheral blood mononuclear cells of prostate cancer patients. These results show for the first time that EphA2 is a tumor rejection antigen and lead us to propose EphA2(58) and EphA2(550) peptides for a broad-spectrum-tumor immunotherapy.

Descriptors: \*HLA-A Antigens--immunology--IM; \*Immunotherapy--methods--MT; \*Neoplasms--therapy--TH; \*Peptide Fragments--immunology--IM; \*Receptor, EphA2--immunology--IM; Animals; CD8-Positive T-Lymphocytes--immunology--IM; COS Cells; Cell Line, Tumor; Cercopithecus aethiops; Epitope Mapping; Epitopes, T-Lymphocyte--immunology--IM; Lymphocyte Activation--immunology--IM; Mice; Mice, Transgenic; Neoplasms--enzymology--EN; Neoplasms--immunology--IM; Peptide Fragments--pharmacology--PD; T-Lymphocytes, Cytotoxic--immunology--IM

CAS Registry No.: 0 (Epitopes, T-Lymphocyte); 0 (HLA-A Antigens); 0 (HLA-A\*0201 antigen); 0 (Peptide Fragments)

Enzyme No.: EC 2.7.1.112 (Receptor, EphA2)

Record Date Created: 20031217

Record Date Completed: 20040227

4/9/3 (Item 3 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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14442366 PMID: 12907621

**Disease stage variation in CD4+ and CD8+ T-cell reactivity to the receptor tyrosine kinase EphA2 in patients with renal cell carcinoma.**

Tatsumi Tomohide; Herrem Christopher J; Olson Walter C; Finke James H; Bukowski Ronald M; Kinch Michael S; Ranieri Elena; Storkus Walter J

Department of Surgery, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213, USA.

Cancer research (United States) Aug 1 2003, 63 (15) p4481-9, ISSN 0008-5472--Print Journal Code: 2984705R

Contract/Grant No.: CA 56937; CA; NCI; CA 57840; CA; NCI

Publishing Model Print

Document type: Journal Article; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

We have evaluated CD8+ and CD4+ T-cell responses against a new tumor-associated antigen, the receptor tyrosine kinase EphA2, which is broadly expressed in diverse cancer histologies and is frequently overexpressed in advanced stage/metastatic disease. We report herein that EphA2 is overexpressed in renal cell carcinoma (RCC) cell lines and clinical specimens of RCC, and find that the highest levels of EphA2 are consistently found in the most advanced stages of the disease. We identified and synthesized five putative HLA class I-binding and three class II-binding peptides derived from EphA2 that might serve as targets for immune reactivity. Each peptide induced specific, tumor-reactive CD8+ or CD4+ T-cell responses as measured using IFN-gamma enzyme-linked immunospot assays. The EphA2 peptides elicited relatively weak responses from CD8+ T cells derived from normal healthy volunteers or from RCC patients with active disease. In marked contrast, immune reactivity to EphA2-derived epitopes was greatly enhanced in CD8+ T cells that had been isolated from patients who were rendered disease-free, after surgery. Furthermore, enzyme-linked immunospot analyses demonstrated prominent EphA2-restricted T-helper 1-type CD4+ T cell activity in patients with early stage disease, whereas T-helper 2-type and T regulatory-type responses predominated in patients with more advanced forms of RCC. These data suggest that the immune system of cancer patients actively monitors EphA2-derived epitopes, and that the magnitude and character of T-cell responses to EphA2 epitopes may convey much-needed predictive information about disease stage and outcome.

Tags: Female; Male

Descriptors: \*CD4-Positive T-Lymphocytes--immunology--IM; \*CD8-Positive T-Lymphocytes--immunology--IM; \*Carcinoma, Renal Cell--immunology--IM; \*Kidney Neoplasms--immunology--IM; \*Receptor, EphA2--immunology--IM; Adult; Aged; Amino Acid Sequence; CD4-Positive T-Lymphocytes--metabolism--ME; CD4-Positive T-Lymphocytes--secretion--SE; CD8-Positive T-Lymphocytes--metabolism--ME; CD8-Positive T-Lymphocytes--secretion--SE; Carcinoma, Renal Cell--metabolism--ME; Carcinoma, Renal Cell--pathology--PA; Epitope Mapping; Epitopes, T-Lymphocyte--immunology--IM; Humans; Interferon Type II--blood--BL; Interferon Type II--secretion--SE; Interleukin-10--biosynthesis--BI; Interleukin-10--blood--BL; Interleukin-5--blood--BL; Interleukin-5--secretion--SE; Kidney Neoplasms--metabolism--ME; Kidney Neoplasms--pathology--PA; Lymphocyte Activation--immunology--IM; Middle Aged; Molecular Sequence Data; Neoplasm Staging; Receptor, EphA2--biosynthesis--BI; Transforming Growth Factor beta--biosynthesis--BI;

Transforming Growth Factor beta--blood--BL  
CAS Registry No.: 0 (Epitopes, T-Lymphocyte); 0 (Interleukin-5); 0  
(Transforming Growth Factor beta); 130068-27-8 (Interleukin-10);  
82115-62-6 (Interferon Type II)  
Enzyme No.: EC 2.7.1.112 (Receptor, EphA2)  
Record Date Created: 20030808  
Record Date Completed: 20030923

4/9/4 (Item 1 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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18591093 BIOSIS NO.: 200510285593

**EphA2 as a glioma-associated antigen: A novel target for glioma vaccines**  
AUTHOR: Hatano Manabu; Eguchi Junichi; Tatsumi Tomohide; Kuwashima Naruo;  
Dusak Jill E; Kinch Michel S; Pollack Ian F; Hamilton Ronald L; Storkus  
Walter J; Okada Hideho (Reprint)  
AUTHOR ADDRESS: Univ Pittsburgh, Dept Neurol Surg, Sch Med, Hillman Canc  
Ctr G12A, 5117 Ctr Ave, Pittsburgh, PA 15213 USA\*\*USA  
AUTHOR E-MAIL ADDRESS: okadah@upmc.edu  
JOURNAL: Neoplasia (New York) 7 (8): p717-722 AUG 2005 2005  
ISSN: 1522-8002  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

**ABSTRACT:** EphA2 is a receptor tyrosine kinase and is frequently overexpressed in a wide array of advanced cancers. We demonstrate in the current study that the EphA2 protein is restrictedly expressed in primary glioblastoma multiforme and anaplastic astrocytoma tissues in comparison to normal brain tissues. To evaluate the possibility of targeting EphA2 in glioma vaccine strategies, we stimulated human leukocyte antigen (HLA) A2(+) peripheral blood mononuclear cells (PBMCs) obtained from healthy donors and glioma patients with autologous dendritic cells (DCs) loaded with synthetic EphA2(883-891) peptide (TLADFDPRV), which has previously been reported to induce interferon-gamma in HLA-A2(+) PBMCs. Stimulated PBMCs demonstrated antigen-specific cytotoxic T lymphocyte (CTL) responses as detected by specific lysis of T2 cells loaded with the EphA2(883) peptide as well as HLA-A2+ glioma cells, SNB19 and U251, that express EphA2. Furthermore, in vivo immunization of HLA-A2 transgenic HHD mice with the EphA2(883-891) peptide resulted in the development of an epitope-specific CTL response in splenocytes, despite the fact that EphA2(883-891) is an autoantigen in these mice. Taken together, these data suggest that EphA2(883-891) may be an attractive antigen epitope for molecularly targeted glioma vaccines.

**DESCRIPTORS:**

**MAJOR CONCEPTS:** Pharmacology; Nervous System--Neural Coordination; Immune System--Chemical Coordination and Homeostasis; Molecular Genetics--Biochemistry and Molecular Biophysics; Tumor Biology  
**BIOSYSTEMATIC NAMES:** Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia  
**ORGANISMS:** SNB19 cell line (Hominidae)--human leukocyte antigen-A2-positive glioma cells; U251 cell line (Hominidae)--human leukocyte antigen-A2-positive glioma cells; mouse (Muridae)--transgenic, strain-HHD

ORGANISMS: PARTS ETC: splenocyte--blood and lymphatics; brain--nervous system; peripheral blood mononuclear cell--immune system, blood and lymphatics; autologous dendritic cell--immune system; antigen-specific cytotoxic T lymphocyte--immune system

COMMON TAXONOMIC TERMS: Humans; Primates; Animals; Chordates; Mammals; Nonhuman Vertebrates; Nonhuman Mammals; Rodents; Vertebrates

DISEASES: glioblastoma multiforme--nervous system disease, neoplastic disease, drug therapy, genetics, prevention and control; anaplastic astrocytoma--nervous system disease, neoplastic disease, drug therapy, genetics, prevention and control

MESH TERMS: Glioblastoma (MeSH); Astrocytoma (MeSH)

CHEMICALS & BIOCHEMICALS: interferon-gamma; human leukocyte antigen-A2; EphA2--overexpression; EphA2-883-891 peptide--antineoplastic-drug, immunostimulant-drug, immunologic-drug, vaccine

GENE NAME: human EphA2 gene (Hominidae) {human receptor tyrosine kinase gene}

CONCEPT CODES:

02506 Cytology - Animal  
02508 Cytology - Human  
03502 Genetics - General  
03506 Genetics - Animal  
03508 Genetics - Human  
10064 Biochemistry studies - Proteins, peptides and amino acids  
12512 Pathology - Therapy  
15002 Blood - Blood and lymph studies  
15004 Blood - Blood cell studies  
20504 Nervous system - Physiology and biochemistry  
20506 Nervous system - Pathology  
22002 Pharmacology - General  
22005 Pharmacology - Clinical pharmacology  
22018 Pharmacology - Immunological processes and allergy  
24003 Neoplasms - Immunology  
24004 Neoplasms - Pathology, clinical aspects and systemic effects  
24008 Neoplasms - Therapeutic agents and therapy  
34502 Immunology - General and methods  
34508 Immunology - Immunopathology, tissue immunology

BIOSYSTEMATIC CODES:

86215 Hominidae  
86375 Muridae

4/9/5 (Item 2 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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17669252 BIOSIS NO.: 200400040009

**EphA2 as target of anticancer immunotherapy: Identification of HLA-A\*0201-restricted epitopes.**

AUTHOR: Alves Pedro M S (Reprint); Faure Olivier; Graff-Dubois Stephanie; Gross David-Alexandre; Cornet Sebastien; Chouaib Salem; Micounnet Isabelle; Lemonnier Francois A; Kosmatopoulos Kostas

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RECORD TYPE: Abstract

LANGUAGE: English

**ABSTRACT:** EphA2 (Eck) is a tyrosine kinase receptor that is overexpressed in several human cancers such as breast, colon, lung, prostate, gastric carcinoma, and metastatic melanoma but not in nonmalignant counterparts. To validate EphA2 as a tumor antigen recognized by CD8+ T lymphocytes, we used reverse immunology approach to identify HLA-A\*0201-restricted epitopes. Peptides bearing the HLA-A\*0201-specific anchor motifs were analyzed for their capacity to bind and stabilize the HLA-A\*0201 molecules. Two peptides, EpbA258 and EphA2550, with a high affinity for HLA-A\*0201 were selected. Both peptides were immunogenic in the HLA-A\*0201-transgenic HHD mice. Interestingly, peptide-specific murine CTLs cell lines responded to COS-7 cells coexpressing HLA-A\*0201 and EphA2 and to EphA2-positive human tumor cells of various origin (renal cell, lung, and colon carcinoma and sarcoma). This demonstrates that EphA258 and EphA2550 are naturally processed from endogenous EphA2. In addition, EphA258, and EphA2550 stimulated specific CD8+ T cells from healthy donor peripheral blood mononuclear cells. These T cells recognized EphA2-positive human tumor cells in an HLA-A\*0201-restricted manner. Interestingly, EphA2-specific CD8+ T cells were detected in the peripheral blood mononuclear cells of prostate cancer patients. These results show for the first time that EphA2 is a tumor rejection antigen and lead us to propose EphA258 and EphA2550 peptides for a broad-spectrum-tumor immunotherapy.

**DESCRIPTORS:**

**MAJOR CONCEPTS:** Biochemistry and Molecular Biophysics; Immune System--Chemical Coordination and Homeostasis

**BIOSYSTEMATIC NAMES:** Cercopithecidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia

**ORGANISMS:** COS-7 cell line (Cercopithecidae)--African green monkey kidney cells; human (Hominidae); mouse (Muridae)

**ORGANISMS: PARTS ETC:** CD8 positive T lymphocyte--immune system; peripheral blood mononuclear cell--blood and lymphatics, immune system

**COMMON TAXONOMIC TERMS:** Nonhuman Primates; Humans; Primates; Animals; Chordates; Mammals; Nonhuman Vertebrates; Nonhuman Mammals; Rodents; Vertebrates

**DISEASES:** colon carcinoma--digestive system disease, neoplastic disease; lung cancer--neoplastic disease, respiratory system disease

**MESH TERMS:** Colonic Neoplasms (MeSH); Carcinoma (MeSH); Lung Neoplasms (MeSH)

**CHEMICALS & BIOCHEMICALS:** EphA2--tyrosine kinase receptor; HLA-A-0201--restricted epitope

**METHODS & EQUIPMENT:** anticancer immunotherapy--clinical techniques, therapeutic and prophylactic techniques; reverse immunology--immunologic techniques, laboratory techniques

**CONCEPT CODES:**

02506 Cytology - Animal

02508 Cytology - Human

10060 Biochemistry studies - General

14006 Digestive system - Pathology

15002 Blood - Blood and lymph studies

15004 Blood - Blood cell studies

16006 Respiratory system - Pathology



24004 Neoplasms - Pathology, clinical aspects and systemic effects

34502 Immunology - General and methods

BIOSYSTEMATIC CODES:

86205 Cercopithecidae

86215 Hominidae

86375 Muridae

4/9/6 (Item 1 from file: 73)

DIALOG(R)File 73:EMBASE

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13828767 EMBASE No: 2006261619

**Design of peptide-based vaccines for cancer**

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Current Medicinal Chemistry ( CURR. MED. CHEM. ) (Netherlands) 2006, 13/14 (1591-1607)

CODEN: CMCHE ISSN: 0929-8673

DOCUMENT TYPE: Journal ; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 205

The immune system responds efficiently to bacteria, viruses and other agents however, the immune response to cancers is not as effective. In most cases other than specific genetic rearrangements leading to non-self proteins such as in leukemia and idiotypes in lymphoma, tumor associated proteins are self proteins and are not recognized by the immune system to prevent malignancy. In most cancers, patients develop antibodies and/or CTL-precursors to tumor associated antigens but are not effective in generating a therapeutic immune response. Adjuvants have been used with either whole tumors, subunits or peptides with the aim of increasing their immunity. Whole tumor antigens have certain advantages associated with it, such as ready availability as recombinant proteins, potential epitopes that can be presented by a number of MHC class I/II alleles and antibody development. The methods of identification of CD8 and CD4 epitopes either by use of epitope prediction algorithms or use of transgenic mice has made the use of defined synthetic peptides more attractive. The possibility to synthesize long peptides and introduce multiple epitopes (CD4 or CD8) from single or multiple antigens makes peptide a viable alternative to whole proteins. As an alternative to totally synthetic peptide constructs or polymers, polytopes have been generated by genetic engineering methods. In addition, to deliver immunogens to and to activate DC, receptor-mediated delivery of peptides using antibodies, cytokines and carbohydrates have been used. This review will encompass the various strategies, preclinical and clinical applications in designing peptide-based vaccines for cancer.

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BRAND NAME/MANUFACTURER NAME: herceptin; rituxan

**DRUG DESCRIPTORS:**

\*cancer vaccine--adverse drug reaction--ae; \*cancer vaccine--clinical trial--ct; \*cancer vaccine--drug analysis--an; \*cancer vaccine--drug development--dv; \*cancer vaccine--drug therapy--dt; \*synthetic peptide--adverse drug reaction--ae; \*synthetic peptide--clinical trial--ct; \*synthetic peptide--drug analysis--an; \*synthetic peptide--drug development--dv; \*synthetic

peptide--drug therapy--dt  
major histocompatibility antigen class 1--endogenous compound--ec; major histocompatibility antigen class 2--endogenous compound--ec; CD4 antigen--endogenous compound--ec; CD8 antigen--endogenous compound--ec; trastuzumab--drug analysis--an; trastuzumab--pharmacology--pd; rituximab--pharmacology--pd; gemtuzumab ozogamicin--drug therapy--dt; dendritic cell vaccine--adverse drug reaction--ae; dendritic cell vaccine--clinical trial--ct; dendritic cell vaccine--drug therapy--dt; NY ESO 1 antigen--adverse drug reaction--ae; NY ESO 1 antigen--clinical trial--ct; NY ESO 1 antigen--drug analysis--an; NY ESO 1 antigen--drug development--dv; NY ESO 1 antigen--drug therapy--dt; mammaglobin--drug development--dv; mammaglobin--drug therapy--dt; ephrin A2--drug therapy--dt; HLA A1 antigen--adverse drug reaction--ae; HLA A1 antigen--clinical trial--ct; HLA A1 antigen--drug therapy--dt; HLA A2 antigen--adverse drug reaction--ae; HLA A2 antigen--clinical trial--ct; HLA A2 antigen--drug therapy--dt; HLA A3 antigen--adverse drug reaction--ae; HLA A3 antigen--clinical trial--ct; HLA A3 antigen--drug therapy--dt; carcinoembryonic antigen--adverse drug reaction--ae; carcinoembryonic antigen--clinical trial--ct; carcinoembryonic antigen--drug therapy--dt; telomerase reverse transcriptase--adverse drug reaction--ae; telomerase reverse transcriptase--clinical trial--ct; telomerase reverse transcriptase--drug therapy--dt; melanoma antigen 3--adverse drug reaction--ae; melanoma antigen 3--clinical trial--ct; melanoma antigen 3--drug therapy--dt; melan A--adverse drug reaction--ae; melan A--clinical trial--ct; melan A--drug therapy--dt; monophenol monooxygenase--adverse drug reaction--ae; monophenol monooxygenase--clinical trial--ct; monophenol monooxygenase--drug therapy--dt; glycoprotein gp 100--adverse drug reaction--ae; glycoprotein gp 100--clinical trial--ct; glycoprotein gp 100--drug therapy--dt; protein p53--endogenous compound--ec; protein antibody--adverse drug reaction--ae; protein antibody--clinical trial--ct; protein antibody--drug therapy--dt; interleukin 2--adverse drug reaction--ae; interleukin 2--clinical trial--ct; interleukin 2--drug therapy--dt; imiquimod--adverse drug reaction--ae; vaccine--adverse drug reaction--ae; vaccine--drug therapy--dt; unclassified drug

**MEDICAL DESCRIPTORS:**

drug design; tumor immunity; antibody production; drug efficacy; prediction; drug synthesis; genetic engineering; cancer immunotherapy; immunological tolerance; epitope mapping; antigen specificity; drug screening; quantitative structure activity relation; B lymphocyte; drug structure; acute granulocytic leukemia--drug therapy--dt; drug response; antineoplastic activity; drug isolation; T lymphocyte; immunogenicity; melanoma--drug therapy--dt; melanoma--prevention--pc; cancer immunization; vitiligo--side effect--si; skin manifestation--side effect--si; autoimmune disease--side effect--si; hypothyroidism--side effect--si; breast cancer--drug therapy--dt; breast cancer--prevention--pc; pancreas cancer--drug therapy--dt; pancreas cancer--prevention--pc; human; nonhuman; clinical trial; review

**DRUG TERMS (UNCONTROLLED):** cpg 7909--adverse drug reaction--ae; cpg 7909--drug therapy--dt

**CAS REGISTRY NO.:** 180288-69-1 (trastuzumab); 174722-31-7 (rituximab); 120178-12-3 (telomerase reverse transcriptase); 9002-10-2 (monophenol monooxygenase); 85898-30-2 (interleukin 2); 99011-02-6 (imiquimod)

**SECTION HEADINGS:**

- 016 Cancer
- 025 Hematology
- 026 Immunology, Serology and Transplantation
- 030 Clinical and Experimental Pharmacology

037 Drug Literature Index  
038 Adverse Reaction Titles

4/9/7 (Item 2 from file: 73)

DIALOG(R)File 73:EMBASE

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13810512 EMBASE No: 2006217052

**EphA2 as a glioma-associated antigen: A novel target for glioma vaccines**

Hatano M.; Eguchi J.; Tatsumi T.; Kuwashima N.; Dusak J.E.; Kinch M.S.; Pollack I.F.; Hamilton R.L.; Storkus W.J.; Okada H.

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Neoplasia ( NEOPLASIA ) (United States) 2005, 7/8 (717-722)

CODEN: NEOPF ISSN: 1522-8002 eISSN: 1476-5586

DOCUMENT TYPE: Journal ; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 17

EphA2 is a receptor tyrosine kinase and is frequently overexpressed in a wide array of advanced cancers. We demonstrate in the current study that the EphA2 protein is restrictedly expressed in primary glioblastoma multiforme and anaplastic astrocytoma tissues in comparison to normal brain tissues. To evaluate the possibility of targeting EphA2 in glioma vaccine strategies, we stimulated human leukocyte antigen (HLA) A2SUP+ peripheral blood mononuclear cells (PBMCs) obtained from healthy donors and glioma patients with autologous dendritic cells (DCs) loaded with synthetic EphA2SUB883-891 peptide (TLADFDPRV), which has previously been reported to induce interferon-gamma in HLA-A2SUP+ PBMCs. Stimulated PBMCs demonstrated antigen-specific cytotoxic T lymphocyte (CTL) responses as detected by specific lysis of T2 cells loaded with the EphA2SUB883 peptide as well as HLA-A2SUP+ glioma cells, SNB19 and U251, that express EphA2. Furthermore, in vivo immunization of HLA-A2 transgenic HHD mice with the EphA2SUB883-891 peptide resulted in the development of an epitope-specific CTL response in splenocytes, despite the fact that EphA2 SUB883-891 is an autoantigen in these mice. Taken together, these data suggest that EphA2SUB883-891 may be an attractive antigen epitope for molecularly targeted glioma vaccines. Copyright (c) 2005 Neoplasia Press, Inc. All rights reserved.

**DRUG DESCRIPTORS:**

\*ephrin receptor A2

HLA A2 antigen--endogenous compound--ec; gamma interferon--endogenous compound--ec; tumor vaccine

**MEDICAL DESCRIPTORS:**

glioblastoma; astrocytoma; peripheral blood mononuclear cell; T lymphocyte; in vivo study; immunization; cytotoxicity; human; nonhuman; mouse; animal experiment; controlled study; human tissue; human cell; article; priority journal

CAS REGISTRY NO.: 82115-62-6 (gamma interferon)

**SECTION HEADINGS:**

016 Cancer

026 Immunology, Serology and Transplantation

4/9/8 (Item 3 from file: 73)

DIALOG(R)File 73:EMBASE

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12412712 EMBASE No: 2003517857

**EphA2 as Target of Anticancer Immunotherapy: Identification of  
HLA-A\*0201-Restricted Epitopes**

Alves P.M.S.; Faure O.; Graff-Dubois S.; Gross D.-A.; Cornet S.; Chouaib  
S.; Miconnet I.; Lemonnier F.A.; Kosmatopoulos K.

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Cancer Research ( CANCER RES. ) (United States) 01 DEC 2003, 63/23  
(8476-8480)

CODEN: CNREA ISSN: 0008-5472

DOCUMENT TYPE: Journal ; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 31

EphA2 (Eck) is a tyrosine kinase receptor that is overexpressed in several human cancers such as breast, colon, lung, prostate, gastric carcinoma, and metastatic melanoma but not in nonmalignant counterparts. To validate EphA2 as a tumor antigen recognized by CD8+ T lymphocytes, we used reverse immunology approach to identify HLA-A\*0201-restricted epitopes. Peptides bearing the HLA-A\*0201-specific anchor motifs were analyzed for their capacity to bind and stabilize the HLA-A\*0201 molecules. Two peptides, EphA2 SUB58 and EphA2SUB550, with a high affinity for HLA-A\*0201 were selected. Both peptides were immunogenic in the HLA-A\*0201-transgenic HHD mice. Interestingly, peptide-specific murine CTLs cell lines responded to COS-7 cells coexpressing HLA-A\*0201 and EphA2 and to EphA2-positive human tumor cells of various origin (renal cell, lung, and colon carcinoma and sarcoma). This demonstrates that EphA2 SUB58 and EphA2SUB550 are naturally processed from endogenous EphA2. In addition, EphA2SUB58 and EphA2SUB550 stimulated specific CD8SUP+ T cells from healthy donor peripheral blood mononuclear cells. These T cells recognized EphA2-positive human tumor cells in an HLA-A\*0201-restricted manner. Interestingly, EphA2-specific CD8+ T cells were detected in the peripheral blood mononuclear cells of prostate cancer patients. These results show for the first time that EphA2 is a tumor rejection antigen and lead us to propose EphA2SUB58 and EphA2 SUB550 peptides for a broad-spectrum-tumor immunotherapy.

**DRUG DESCRIPTORS:**

\*ephrin A2--endogenous compound--ec; \*HLA A antigen--endogenous compound  
--ec

epitope--endogenous compound--ec

**MEDICAL DESCRIPTORS:**

\*cancer immunotherapy

gene overexpression; breast cancer; colon cancer; lung cancer; prostate  
cancer; stomach cancer; melanoma; T lymphocyte; antigen recognition;  
protein binding; protein stability; cell strain COS7; antigen expression;  
kidney carcinoma; sarcoma; protein processing; peripheral blood mononuclear  
cell; tumor rejection; transgenic mouse; cytotoxic T lymphocyte; human;  
nonhuman; mouse; human cell; animal cell; article; priority journal

**SECTION HEADINGS:**

016 Cancer

026 Immunology, Serology and Transplantation

4/9/9 (Item 4 from file: 73)

DIALOG(R)File 73:EMBASE

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12219347 EMBASE No: 2003319481

**Disease stage variation in CD4+ and CD8+ T-cell reactivity to the receptor tyrosine kinase EphA2 in patients with renal cell carcinoma**

Tatsumi T.; Herrem C.J.; Olson W.C.; Finke J.H.; Bukowski R.M.; Kinch M.S.; Ranieri E.; Storkus W.J.

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AUTHOR EMAIL: storkuswj@msx.upmc.edu

Cancer Research ( CANCER RES. ) (United States) 01 AUG 2003, 63/15 (4481-4489)

CODEN: CNREA ISSN: 0008-5472

DOCUMENT TYPE: Journal ; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 56

We have evaluated CD8+ and CD4+ T-cell responses against a new tumor-associated antigen, the receptor tyrosine kinase EphA2, which is broadly expressed in diverse cancer histologies and is frequently overexpressed in advanced stage/metastatic disease. We report herein that EphA2 is overexpressed in renal cell carcinoma (RCC) cell lines and clinical specimens of RCC, and find that the highest levels of EphA2 are consistently found in the most advanced stages of the disease. We identified and synthesized five putative HLA class I-binding and three class II-binding peptides derived from EphA2 that might serve as targets for immune reactivity. Each peptide induced specific, tumor-reactive CD8+ or CD4+ T-cell responses as measured using IFN-gamma enzyme-linked immunospot assays. The EphA2 peptides elicited relatively weak responses from CD8+ T cells derived from normal healthy volunteers or from RCC patients with active disease. In marked contrast, immune reactivity to EphA2-derived epitopes was greatly enhanced in CD8+ T cells that had been isolated from patients who were rendered disease-free, after surgery. Furthermore, enzyme-linked immunospot analyses demonstrated prominent EphA2-restricted T-helper 1-type CD4+ T cell activity in patients with early stage disease, whereas T-helper 2-type and T regulatory-type responses predominated in patients with more advanced forms of RCC. These data suggest that the immune system of cancer patients actively monitors EphA2-derived epitopes, and that the magnitude and character of T-cell responses to EphA2 epitopes may convey much-needed predictive information about disease stage and outcome.

;

MOLECULAR SEQUENCE NUMBER: GENBANK, XP048780

**DRUG DESCRIPTORS:**

\*CD4 antigen; \*CD8 antigen; \*tyrosine kinase receptor; \*synthetic peptide cytokine; gamma interferon; interleukin 5; transforming growth factor beta; HLA DR4 antigen; HLA A2 antigen; epitope; unclassified drug

**MEDICAL DESCRIPTORS:**

\*kidney carcinoma--etiology--et; \*T lymphocyte; \*nucleotide sequence tumor immunology; HLA typing; Western blotting; immunohistochemistry; peptide synthesis; enzyme linked immunosorbent assay; human; controlled study; human cell; article; priority journal

DRUG TERMS (UNCONTROLLED): EphA2 protein  
CAS REGISTRY NO.: 82115-62-6 (gamma interferon)

## SECTION HEADINGS:

- 016 Cancer
- 026 Immunology, Serology and Transplantation
- 028 Urology and Nephrology
- 029 Clinical and Experimental Biochemistry

4/9/10 (Item 1 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

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14474362 Genuine Article#: 976AY Number of References: 17

**Title: EphA2 as a glioma-associated antigen: A novel target for glioma vaccines**

Author(s): Hatano M; Eguchi J; Tatsumi T; Kuwashima N; Dusak JE; Kinch MS; Pollack IF; Hamilton RL; Storkus WJ; Okada H (REPRINT)

Corporate Source: Univ Pittsburgh, Dept Neurol Surg, Sch Med, Hillman Canc Ctr G12A, 5117 Ctr Ave/Pittsburgh//PA/15213 (REPRINT); Univ Pittsburgh, Dept Neurol Surg, Sch Med, Hillman Canc Ctr G12A, Pittsburgh//PA/15213; Univ Pittsburgh, Inst Canc, Pittsburgh//PA/15213; Osaka Univ, Dept Mol Therapeut, Osaka//Japan//; MedImmune Inc, Gaithersburg//MD//; Univ Pittsburgh, Dept Pathol, Sch Med, Pittsburgh//PA/15213; Univ Pittsburgh, Dept Dermatol, Sch Med, Pittsburgh//PA/15213; Univ Pittsburgh, Dept Surg, Sch Med, Pittsburgh//PA/15213(okadah@upmc.edu)

Journal: NEOPLASIA, 2005, V7, N8 (AUG), P717-722

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Publisher: B C DECKER INC, 20 HUGHSON ST SOUTH, PO BOX 620, L C D 1, HAMILTON, ONTARIO L8N 3K7, CANADA

Language: English Document Type: ARTICLE

Geographic Location: USA; Japan

Journal Subject Category: ONCOLOGY

**Abstract:** EphA2 is a receptor tyrosine kinase and is frequently overexpressed in a wide array of advanced cancers. We demonstrate in the current study that the EphA2 protein is restrictedly expressed in primary glioblastoma multiforme and anaplastic astrocytoma tissues in comparison to normal brain tissues. To evaluate the possibility of targeting EphA2 in glioma vaccine strategies, we stimulated human leukocyte antigen (HLA) A2(+) peripheral blood mononuclear cells (PBMCs) obtained from healthy donors and glioma patients with autologous dendritic cells (DCs) loaded with synthetic EphA2(883-891) peptide (TLADFDPRV), which has previously been reported to induce interferon-gamma in HLA-A2(+) PBMCs. Stimulated PBMCs demonstrated antigen-specific cytotoxic T lymphocyte (CTL) responses as detected by specific lysis of T2 cells loaded with the EphA2(883) peptide as well as HLA-A2+ glioma cells, SNB19 and U251, that express EphA2. Furthermore, in vivo immunization of HLA-A2 transgenic HHD mice with the EphA2(883-891) peptide resulted in the development of an epitope-specific CTL response in splenocytes, despite the fact that EphA2(883-891) is an autoantigen in these mice. Taken together, these data suggest that EphA2(883-891) may be an attractive antigen epitope for molecularly targeted glioma vaccines.

**Descriptors--Author Keywords:** EphA2 ; glioma ; cancer vaccine ; cytotoxic T lymphocytes ; human leukocyte antigen (HLA) A2

**Identifiers--KeyWord Plus(R):** RENAL-CELL CARCINOMA; AUTOLOGOUS GLIOMA;

TYROSINE KINASE; IMMUNOTHERAPY; VACCINATION; RECEPTOR; OVEREXPRESSION;  
IDENTIFICATION; GLIOBLASTOMA; FIBROBLASTS

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Set	Items	Description
S1	6271	(EPHA2 OR ECK OR EPHRIN)
S2	16	S1 AND (HLA AND PEPTIDE)
S3	13	S2 AND (EPITOPE)
S4	10	S3 AND (T (N) (CELL OR LYMPHOCYTE))

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1402 EPHRIN

652 EPHRINS

1562 EPHRIN

(EPHRIN OR EPHRINS)

582 ECK

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585 ECK

(ECK OR ECKS)

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2285124 CELL

1980623 CELLS

3000378 CELL

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Bruijnzeel-Koomen, C. A. F. M.; Tilanus, M. G.; Knol, E. F.; van Hoffen,  
E.CS Department of Dermatology/Allergology, University Medical Center, Utrecht,  
Neth.SO International Archives of Allergy and Immunology (2007), 143(2), 119-126  
CODEN: IAAIEG; ISSN: 1018-2438

PB S. Karger AG

DT Journal

LA English

AB Background: Little is known about the assocn. between human leukocyte antigen (HLA) and cow's milk allergy (CMA). The aim of the present study was to det. the HLA restriction of T cell clones (TCCs) specific to  $\alpha$ s1-casein, the most abundant milk protein, and to study possible HLA class II allele assocns. with CMA. Methods:  $\alpha$ s1-Casein-specific TCCs were derived from 6 children with CMA, 9 atopic children without CMA and 5 non-atopic children. T cell epitope specificity was defined by stimulation with overlapping peptides, spanning the  $\alpha$ s1-casein mol. HLA restriction was detd. in proliferation assays using antibodies blocking either HLA-DP, HLA-DQ or HLA-DR. HLA genotyping was performed in 32 subjects with CMA, 23 atopic and 22 non-atopic individuals. Results: Ten TCCs were restricted to HLA-DQ, 6 TCCs to HLA-DR and 4 TCCs to HLA-DP. The sequence in  $\alpha$ s1-casein that was most immunogenic to T cells from children with CMA contained T cell epitopes restricted to DQB1\*0201, DPB1\*0401 and DRB1\*1501. The DQB1\*0501 allele frequency was lower in children with CMA than in non-atopic children, but this difference could not be confirmed in an addnl. group of subjects with and without CMA. Conclusions: HLA-DQ plays a substantial role in the

presentation of **T cell epitopes** in  $\alpha$ s1-casein. However, **HLA** class II allele frequencies do not show major differences between cow's milk allergic, atopic and non-atopic subjects. **T cell epitopes** in the most immunogenic region are presented by various abundantly present **HLA** genotypes. Therefore, this sequence may be a suitable target for **peptide** immunotherapy.

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text	Citing References
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AN 2006:766261 CAPLUS

DN 145:354147

TI Screening and Identification of Severe Acute Respiratory Syndrome-Associated Coronavirus-Specific CTL **Epitopes**

AU Zhou, Minghai; Xu, Dongping; Li, Xiaojuan; Li, Hongtao; Shan, Ming; Tang, Jiaren; Wang, Min; Wang, Fu-Sheng; Zhu, Xiaodong; Tao, Hua; He, Wei; Tien, Po; Gao, George F.

CS Center for Molecular Immunology, Center for Molecular Virology, Institute of Microbiology, Chinese Academy of Sciences (CAS), Beijing, Peop. Rep. China

SO Journal of Immunology (2006), 177(4), 2138-2145  
CODEN: JOIMA3; ISSN: 0022-1767

PB American Association of Immunologists

DT Journal

LA English

AB Severe acute respiratory syndrome (SARS) is a highly contagious and life-threatening disease that emerged in China in Nov. 2002. A novel SARS-assocd. coronavirus was identified as its principal etiol. agent; however, the immunopathogenesis of SARS and the role of special CTLs in virus clearance are still largely uncharacterized. In this study, potential **HLA-A\*0201**-restricted spike (S) and nucleocapsid protein-derived **peptides** were selected from an online database and screened for potential CTL **epitopes** by in vitro refolding and T2 cell-stabilization assays. The antigenicity of nine **peptides** which could refold with **HLA-A\*0201** mols. was assessed with an IFN- $\gamma$  ELISPOT assay to det. the capacity to stimulate CTLs from PBMCs of **HLA-A2+** SARS-recovered donors. A novel **HLA-A\*0201**-restricted decameric **epitope** P15 (S411-420, KLPDDFMGCV) derived from the S protein was identified and found to localize within the angiotensin-converting enzyme 2 receptor-binding region of the S1 domain. P15 could significantly enhance the expression of **HLA-A\*0201** mols. on the T2 cell surface, stimulate IFN- $\gamma$ -producing CTLs from the PBMCs of former SARS patients, and induce specific CTLs from P15-immunized **HLA-A2.1** transgenic mice in vivo. Furthermore, significant P15-specific CTLs were induced from **HLA-A2.1**-transgenic mice immunized by a DNA vaccine encoding the S protein; suggesting that P15 was a naturally processed **epitope**. Thus, P15 may be a novel SARS-assocd. coronavirus-specific CTL **epitope** and a potential target for characterization of virus control mechanisms and evaluation of candidate SARS vaccines.

RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text	Citing References
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AN 2006:642722 CAPLUS  
 DN 145:122486  
 TI High-Affinity Interactions between **Peptides** and Heat Shock Protein 70  
 Augment CD8+ **T Lymphocyte** Immune Responses  
 AU Flechtner, Jessica B.; Cohane, Kenya Prince; Mehta, Sunil; Slusarewicz,  
 Paul; Leonard, Alexis Kays; Barber, Brian H.; Levey, Daniel L.; Andjelic,  
 Sofija  
 CS Antigenics Inc., Lexington, MA, 02421, USA  
 SO Journal of Immunology (2006), 177(2), 1017-1027  
 CODEN: JOIMA3; ISSN: 0022-1767  
 PB American Association of Immunologists  
 DT Journal  
 LA English  
 AB Exogenously delivered antigenic **peptides** complexed to heat shock  
 proteins (HSPs) are able to enter the endogenous Ag-processing pathway and  
 prime CD8+ CTL. It was detd. previously that a hybrid **peptide** contg. a  
 MHC class I-binding **epitope** and HSP70-binding sequence Javelin (J0) in  
 complex with HSP70 could induce cytotoxic **T cell** responses in vivo  
 that were more robust than those induced by the minimal **epitope**  
 complexed with HSP70. The present study introduces a novel,  
 higher-affinity HSP70-binding sequence (J1) that significantly enhances  
 binding of various antigenic **peptides** to HSP70. A competition binding  
 assay revealed a dissocn. const. that was 15-fold lower for the H2-Kb OVA  
**epitope** SIINFEKL-J1 compared with SIINFEKL-J0, indicating a  
 substantially higher affinity for HSP70. Further, modifying the  
 orientation of the hybrid **epitope** and introducing a cleavable linker  
 sequence between the Javelin and the **epitope** results in even greater  
 immunogenicity, presumably by greater efficiency of **epitope** processing.  
 The enhanced immunogenicity assocd. with Javelin J1 and the cleavable  
 linker is consistently obsd. with multiple mouse and human **epitopes**.  
 Thus, by creating a series of **epitopes** with uniform, high-affinity  
 binding to HSP70, successful multiple **epitope** immunizations are  
 possible, with equal delivery of each antigenic **epitope** to the immune  
 system via HSP70. These modified **epitopes** have the potential for  
 creating successful multivalent vaccines for immunotherapy of both  
 infectious disease and cancer.

RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text	Citing References
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AN 2006:927229 CAPLUS  
 DN 146:120234  
 TI Identification of HLA-DRB1\* 07-restricted **T cell epitope** on keratin 17  
 AU Shen, Zhu; Wang, Gang; Liu, Yufeng; Li, Wei; Fan, Jianyong; Dang, Yuping  
 CS Xijing Hospital, Fourth Military Medical University, Xian, Shanxi  
 Province, 710032, Peop. Rep. China  
 SO Zhonghua Weishengwuxue He Mianyixue Zazhi (2005), 25(10), 790-793  
 CODEN: ZWMZDP; ISSN: 0254-5101  
 PB Beijing Shengwu Zhipin Yanjiuso  
 DT Journal  
 LA Chinese  
 AB The HIA-DRB1 \* 07-restricted **T cell epitopes** on keratin 17 (K17),  
 one of the autoantigens of psoriasis was identified. Methods In the

previous study we identified the **HLA-DRB1 \* 07-restricted T cell epitope** regions on K17. **Epitopes** in the regions were predicted with internet servers in this study. The two nucleic acid strains of each predicted **epitope** with restriction endonuclease sites were synthesized and then expressed at N-terminus of GST. These recombinant **epitopes** and the level of **T cell** proliferation and the concn. of IFN- $\gamma$  in the culture were detected. Compared with the control group and other **epitopes**, S1 (118-132), S2 (169-183), S3 (323-337) and S4 (348-362) had a pos. role on the proliferation and IFN- $\gamma$  expression of **T cells** from psoriatic patients. The results indicated that **epitopes S1** (118-132)(VRALEEANTELEVKI), S2 (169-183)(ANILLQIDNARLAAD), S3 (323-337)(MQALEIELQSQLSMK) and S4 (348-362)(ENRYCVQLSQIQGLI) are the psoriasis-specific **HLA-DRB1 \* 07-restricted T cell epitopes**. The advanced study targeting to these **peptides** can provide a more complete understanding of the immunol. basis of the disease.

L5 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN



AN 2005:282930 CAPLUS  
 DN 143:42392  
 TI **HLA-DRB1\*04, \*07-restricted epitopes** on Keratin 17 for autoreactive **T cells** in psoriasis  
 AU Shen, Z.; Wang, G.; Fan, J.-Y.; Li, W.; Liu, Y.-F.  
 CS Department of Dermatology, Fourth Military Medical University, Xi'an, 710032, Peop. Rep. China  
 SO Journal of Dermatological Science (2005), 38(1), 25-39  
 CODEN: JDSCEI; ISSN: 0923-1811  
 PB Elsevier Ireland Ltd.  
 DT Journal  
 LA English  
 AB Psoriasis is a **T cell**-mediated inflammatory skin disease. Recent evidence suggests that activated CD4+ helper **T lymphocytes** of the Th1 phenotype play an important role in the pathogenesis of the disease. For psoriatic autoreactive **T cells**, Keratin 17 is a major target antigen and an **epitope** contg. ALEEAN sequence has been described, but other psoriasis-related **epitopes** are still unknown. To identify the **HLA DRB1\*04, \*07-restricted T cell epitopes** on Keratin 17. **HLA DRB1\*04, \*07-restricted T cell epitope** regions on Keratin 17 were predicted based on related softwares and internet servers. Keratin 17 gene was amplified from psoriatic epidermis and the proteins of the predicted **epitope** regions were expressed, identified and purified. **T cells** from psoriatic patients reacted in cultivation with **peptide**-major histocompatibility complex (p-MHC) compd., then the level of **cell** proliferation and the concn. of interferon- $\gamma$  in culture supernatant were detected. After the psoriasis-related **epitope** regions were narrowed down, the **epitopes** on them were predicted further. These **epitopes** were then expressed and validated by **T cell** response in vitro. Results:: Four **epitopes-S1** (118-132), S2 (169-183), S3 (323-337) and S4 (348-362) can stimulate the proliferation and interferon- $\gamma$  prodn. of psoriatic **T cells** more effectively than other **epitopes** and react weakly with the **T cells** from healthy volunteers. **Epitopes S1** (118-132), S2 (169-183), S3 (323-337) and S4 (348-362) are immunodominant DRB1-restricted **T cell epitopes** for psoriasis. Among them, S1 (118-132) contains the ALEEAN sequence while the others with different amino acid sequence have not been reported before. Further studies based on these **peptides** would provide a more

complete understanding of the immunol. basis of psoriasis.

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text	Citing References
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AN 2002:937303 CAPLUS

DN 138:20443

TI Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes

IN Kondo, Akihiro; Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto, Yoshimasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunoshin

PA Takara Bio Inc., Japan

SO Jpn. Kokai Tokkyo Koho, 386 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	<u>JP 2002355079</u>	A	20021210	<u>JP 2002-69354</u>	20020313
PRAI	<u>JP 2001-73183</u>	A	20010314		
	<u>JP 2001-74993</u>	A	20010315		
	<u>JP 2001-102519</u>	A	20010330		

AB A method and kit for detecting endocrine-disrupting chems. using DNA microarrays are claimed. The method comprises prep. a nucleic acid sample contg. mRNAs or cDNAs originating in cells, tissues, or organisms which have been brought into contact with a sample contg. the endocrine disruptor. The nucleic acid sample is hybridized with DNA microarrays having genes affected by the endocrine disruptor or DNA fragments originating in these genes have been fixed. The results obtained are then compared with the results obtained with the control sample to select the gene affected by the endocrine disruptor. Genes whose expression is altered by tri-Bu tin, 4-octaphenol, 4-nonylphenol, di-N-Bu phthalate, dichlorohexyl phthalate, octachlorostyrene, benzophenone, diethylhexyl phthalate, diethylstilbestrol (DES), and 17- $\beta$  estradiol (E2), were found in mice by DNA chip anal.

L5 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text	Citing References
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AN 2002:223044 CAPLUS

DN 137:123984

TI Resolution of chronic hepatitis B and anti-HBs seroconversion in humans by adoptive transfer of immunity to hepatitis B core antigen

AU Lau, George K. K.; Suri, Deepak; Liang, Raymond; Rigopoulou, Eirini I.; Thomas, Mark G.; Mullerova, Ivana; Nanji, Amin; Yuen, Siu-Tsan; Williams, Roger; Naoumov, Nikolai V.

CS Institute of Hepatology, University College London, London, UK

SO Gastroenterology (2002), 122(3), 614-624

CODEN: GASTAB; ISSN: 0016-5085

PB W. B. Saunders Co.

DT Journal

LA English

AB Impaired T-cell reactivity is believed to be the dominant cause of chronic hepatitis B virus (HBV) infection. We characterized HBV-specific

**T-cell** responses in chronic hepatitis B surface antigen carriers who received bone marrow from **HLA**-identical donors with natural immunity to HBV and seroconverted to antibody to hepatitis B surface antigen. **T-cell** reactivity to HBV antigens and **peptides** was assessed in a proliferation assay, the frequency of HBV core- and surface-specific **T cells** was quantified directly by ELISPOT assays, and **T-cell** subsets were analyzed by flow cytometry. CD4+ **T-cell** reactivity to HBV core was common in bone marrow donors and the corresponding recipients after hepatitis B surface antigen clearance, whereas none reacted to surface, pre-S1, or pre-S2 antigens. Furthermore, CD4+ **T cells** from donor/recipient pairs recognized similar **epitopes** on hepatitis B core antigen; using polymerase chain reaction for the Y chromosome, the recipients' CD4+ **T lymphocytes** were confirmed to be of donor origin. The frequency of core-specific CD4+ and CD8+ **T cells** was several-fold higher than those specific for surface antigen. This study provides the first evidence in humans that transfer of hepatitis B core antigen-reactive **T cells** is assocd. with resoln. of chronic HBV infection. Therapeutic immunization with HBV core gene or protein deserves further investigation in patients with chronic hepatitis B.

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text	Citing References
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AN 2001:263061 CAPLUS

DN 135:32504

TI In vitro binding analysis of hepatitis B virus preS-derived putative helper **T-cell epitopes** to MHC class II molecules using stable **HLA-DRB1\*0405/-DRA\*0101** transfected cells

AU Kim, Jung-Hwan; Park, Jung-Hyun; Lee, Yun-Jung; Cho, Eun-Wie; Bae, Yong-Soo; Kim, Kil Lyong

CS Protein Engineering Laboratory, Korea Research Institute of Bioscience and Biotechnology, Taejon, 305-600, S. Korea

SO IUBMB Life (2000), 50(6), 379-384

CODEN: IULIF8; ISSN: 1521-6543

PB Taylor & Francis

DT Journal

LA English

AB In designing **epitope**-based vaccines, the inclusion of a helper **T-lymphocyte** (HTL) **epitope** is necessary to elicit both humoral and cellular immune responses. Whereas the preS region of the hepatitis B virus (HBV) surface antigen is well-known to raise protective immunity, the **epitopes** for activating HTLs are poorly characterized. In an attempt to identify such **epitopes**, the HBV-preS region was screened for **peptide** sequences with **HLA-DR4** binding motifs, and putative HTL candidate **peptides** were synthesized in a biotinylated form. Using L929 mouse fibroblasts stably transfected with **HLA-DRB1\*0405** and **HLA-DRA\*0101** cDNA, specific binding of the **peptides** was then detected using fluorescence-conjugated streptavidin. The cell-surface expression of **HLA-DR** mols. on transfectants was confirmed by confocal microscopy, and quant. anal. of candidate **peptide** binding was performed by fluorescence activated cell sorting. Among eight preS-derived **peptides**, three candidate **peptides**, namely preS1(23-33), preS1(62-72), and preS1(76-86), showed good binding characteristics to **HLA-DR4** mols., among which the preS1(23-33) **epitope** was regarded as the most promising HTL **epitope**. Further studies with these candidate HTL stimulatory

**peptides** will show their ability to activate the human immune system against HBV.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text	Citing References
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AN 1999:668303 CAPLUS

DN 132:34396

TI Induction of CD4+ and CD8+ Bordetella pertussis toxin subunit S1 specific **T cells** by immunization with synthetic **peptides**

AU Fagerberg, Jan; Askelof, Per; Wigzell, Hans; Mellstedt, Haakan

CS Department of Oncology (Radiumhemmet), Karolinska Hospital, Stockholm, S-171 77, Swed.

SO Cellular Immunology (1999), 196(2), 110-121

CODEN: CLIMB8; ISSN: 0008-8749

PB Academic Press

DT Journal

LA English

AB In this study two synthetic **peptides** from the Bordetella pertussis toxin subunit S1 were conjugated to human anti-idiotypic antibodies and used as an immunogen in cancer patients to induce immunity. The aims of the present report are to explain why no carrier or adjuvant effect of the conjugated pertussis **peptides** could be established regarding induction of responses against the anti-idiotypic and to explore the type and quality of induced anti-pertussis immune responses. The lack of carrier and adjuvant effect of the **peptides** might be related to the fact that the anti-idiotypic antibodies by themselves include helper **epitopes** and that none of the patients had a detectable **T cell** response against any of the selected **peptides** before immunization, which might be a requirement for an adjuvant effect. However, three of four immunized patients mounted a humoral as well as cellular response against the pertussis **peptides** used. The induced **T cell** immunity was restricted to one of the two **peptides** in responding patients. Established **T cell** lines and MHC blocking studies indicated that the **T cell epitopes** of the two **peptides** had a different MHC restriction. The type of **T cell** response induced seemed to govern the humoral response. The only durable antibody response was accompanied by the presence of a CD4+ **T cell** response against the same **peptide**. Immunization with an anti-idiotypic conjugated to synthetic **peptides** might thus induce both a B and a **T cell** response against the **peptides** and the type of induced **T cells** (CD4 or CD8) governs the quality of the humoral response. Moreover, the possibility of boosting or inducing a response against the antigen from which the **peptide** sequences were deduced also seemed feasible. (c) 1999 Academic Press.

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text	Citing References
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AN 1997:408150 CAPLUS

DN 127:148307

TI Production of both IFN- $\gamma$  and IL-5 by Onchocerca volvulus S1 antigen-specific CD4+ **T cells** from putatively immune individuals

AU Doetze, Andrea; Erttmann, Klaus D.; Gallin, Michaela Y.; Fleischer,



Bernhard; Hoerauf, Achim  
 CS Departments Immunol. Mol. Biol., Bernhard-Nocht-Inst. Tropical Med.,  
 Hamburg, 20359, Germany  
 SO International Immunology (1997), 9(5), 721-729  
 CODEN: INIMEN; ISSN: 0953-8178  
 PB Oxford University Press  
 DT Journal  
 LA English  
 AB Protective immunity to the parasitic nematode *Onchocerca volvulus* (Ov) appears to be directed against mols. of invading L3 larvae. In this study, the cellular immune reaction to such an Ov L3 protein (S1) which is protective in an animal model was analyzed using peripheral blood mononuclear cells (PBMC) of individuals from a hyperendemic area in West Africa who were exposed to Ov but remained free from disease ('putatively immune individuals'). Despite seronegativity of these individuals against S1, proliferation of PBMC was inducible, allowing generation of an S1-specific T cell line which produced IFN- $\gamma$  upon stimulation with both Ov lysate and S1. However, S1 induced significantly more IL-5 than Ov lysate. S1-specific, DQ6 (DQA1\*0103DQB1\*0603)-restricted T cell clones were generated which reacted against synthetic peptides comprising amino acids 99-111 of S1. These clones, which are the first generated against a recombinant filarial antigen, produced both IFN- $\gamma$  and IL-5 as well as little IL-4, suggestive of a Th0-like phenotype. In conclusion, in putative immunity, reactivity against a particular parasite protein can be detectable on the level of T but not B cells. Induction of both IFN- $\gamma$  and IL-5 by S1 suggests that it may trigger macrophage plus eosinophil dependent killing of L3 in vivo. The identification of a likely DQ6 (DQA1\*0103/DQB1\*0603)-restricted T cell epitope may be of more general relevance, given that allele combinations of DQ6, including DQA1\*0103/DQB1\*0603, are neg. assocd. with diabetes mellitus.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text	Citing References
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AN 1992:509645 CAPLUS  
 DN 117:109645  
 TI Interaction of a T-cell epitope of pertussis toxin with the molecules of the immune system  
 AU Di Tommaso, A.; Oksenberg, J. R.; Steinman, L.; Judd, A. K.; Sette, A.; Karr, R. W.; Olson, R.; Fu, X. T.; Rappuoli, R.; De Magistris, M. T.  
 CS Sclavo Res. Cent., Siena, 53100, Italy  
 SO Zentralblatt fuer Bakteriologie, Supplement (1992), 23(Bact. Protein Toxins), 377-84  
 CODEN: ZBASE2; ISSN: 0941-018X  
 DT Journal  
 LA English  
 AB The peptide 20-42 (p30-42) of the S1 subunit of pertussis toxin has been previously shown to be immunodominant in DR1 individuals. Immunity against this peptide has been detected following whooping cough and after vaccination with acellular pertussis vaccines. The authors analyzed at the mol. level the interaction of p30-42 with the major histocompatibility complex (MHC) mols. and with the T cell receptor (TCR) of 9 human T cell clones specific for the peptide. A series of alanine-substituted analogs of p30-42 were synthesized and tested their

ability to bind purified DR1 mols. and to stimulate **T cell** proliferation, using antigen presenting **cells** (APC) contg. wild type DR1 mols., or DR1 mols. mutagenized by site-directed mutagenesis in the  $\alpha$  and  $\beta$  chains. A map of the fine interactions between the amino acids of the immunogenic **peptide** and those of the MHC mols. has been constructed.

L5 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text	Citing References
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AN 1992:529506 CAPLUS

DN 117:129506

TI Fine specificity of the human **T-cell** response to the hepatitis B virus preS1 antigen

AU Ferrari, Carlo; Cavalli, Albertina; Penna, Amalia; Valli, Antonietta; Bertoletti, Antonio; Pedretti, Giovanni; Pilli, Massimo; Vitali, Piero; Neri, Tauro M.; et al.

CS Univ. Parma, Parma, Italy

SO Gastroenterology (1992), 103(1), 255-63  
CODEN: GASTAB; ISSN: 0016-5085

DT Journal

LA English

AB The **T-cell** response to hepatitis B virus envelope antigens was studied in 11 hepatitis B vaccine recipients; 7 were selected to analyze the fine specificity of the **T-cell** response to the preS1 antigen. Four distinct **T-cell epitopes** were identified by peripheral blood lymphomononuclear **cell** stimulation with a panel of short synthetic **peptides** covering the preS1 sequence. The immunodominance of the preS1 **epitopes** included within **peptides** 21-30 and 29-48 was shown by their capacity to restimulate an **HLA** class I restricted proliferative response of **T cells** primed with the whole preS1 antigen. Conversely, **peptide-specific T cells** selected by peripheral blood lymphomononuclear **cell** stimulation with **peptides** 21-30 and 29-48 were able to recognize the native preS1 mol., confirming that these **epitopes** are actually generated by the intracellular processing of preS1. Finally, amino acid residues essential for **T-cell** activation by **peptide** 21-30 were identified by using 10 analogs of the stimulatory **peptide** contg. single alanine substitutions. These results may be relevant to the design of efficient synthetic vaccines against hepatitis B virus infection.

L5 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text	Citing References
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AN 1989:437521 CAPLUS

DN 111:37521

TI Human **T cell** clones define **S1** subunit as the most immunogenic moiety of pertussis toxin and determine its **epitope** map

AU De Magistris, M. Teresa; Romano, Miriam; Bartoloni, Antonella; Rappuoli, Rino; Tagliabue, Aldo

CS Sclavo Res. Cent., Siena, 53100, Italy

SO Journal of Experimental Medicine (1989), 169(5), 1519-32  
CODEN: JEMEAV; ISSN: 0022-1007

DT Journal

LA English

AB Human **T lymphocyte** clones specific for pertussis toxin (PT) were used to analyze the fine specificity of the response to PT, the basic component of new acellular vaccines against whooping cough. The majority (83%) of

the clones specific for PT recognized **S1**, the subunit that in animal models has been shown to be highly immunogenic. To map **T cell epitopes** on **S1**, 18 **S1**-specific clones were tested for recognition of recombinant fragments representing N-terminal and C-terminal deletions of **S1** and two recombinant **S1** subunits contg. amino acid substitutions. This approach led to the identification of three regions of the protein as the sequences contg. **T cell** antigenic sites: 1-42, 181-211, and 212-235. Synthetic **peptides** were eventually used for a finer localization of the **T cell epitopes**. Two **peptides**, one of 13 residues (27-39) at the N-terminus and one of 24 residues (171-194) at the C-terminus, stimulated proliferation of three and four clones, resp. Both **peptides** are recognized in assocn. with **HLA-DR1** mols. These results stress the role of **S1** in the immune response to PT and provide data useful for the development of a recombinant or synthetic antipertussis vaccine contg. **T cell epitopes** from **S1**.

L5 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN



AN 1989:37472 CAPLUS

DN 110:37472

TI MHC-restricted recognition of immunogenic **T cell epitopes** of pertussis toxin reveals determinants in man distinct from the ADP-ribosylase active site

AU Oksenberg, Jorge R.; Judd, Amrit K.; Ko, Cynthia; Lim, Mae; Fernandez, Rosmary; Schoolnik, Gary K.; Steinman, Lawrence

CS Dep. Neurol., Stanford Univ., Stanford, CA, 94305, USA

SO Journal of Experimental Medicine (1988), 168(5), 1855-64  
CODEN: JEMEAU; ISSN: 0022-1007

DT Journal

LA English

AB The **S1** subunit of pertussis toxin (PT) is responsible for the reactogenicity and in part the immunogenicity of Bordetella pertussis vaccine. The crit. residues assocd. with the immunomodulatory effects of PT were located around Glu140 in the **S1** subunit. In man, **T cell** responses to PT are directed at **S1 peptides** distinct from Glu140. Two such **epitopes**, p64-75 and p151-161, are immunogenic in a panel of individuals covering a wide range of **HLA** genotypes. The response to PT **peptides** is **HLA** class II restricted. The response to p64-75 is blocked by an anti-**HLA-DQ** mAb, while that to p151-161 is blocked by an anti-**HLA-DR** mAb. These findings may allow for the development of a B. pertussis vaccine free from reactogenicity.

=> s L1 and (HLA and peptide)

36735 HLA

80 HLAS

36754 HLA

(HLA OR HLAS)

380732 PEPTIDE

277148 PEPTIDES

485707 PEPTIDE

(PEPTIDE OR PEPTIDES)

L6 51 L1 AND (HLA AND PEPTIDE)

=> s L6 and (epitope)

41639 EPITOPE

43335 EPITOPES

63137 EPITOPE

(EPITOPE OR EPITOPES)

L7 11 L6 AND (EPITOPE)

=&gt; s L7 and (T and (cell or lymphocyte))

886799 T

2285124 CELL

1980623 CELLS

3000378 CELL

(CELL OR CELLS)

227576 LYMPHOCYTE

122263 LYMPHOCYTES

258547 LYMPHOCYTE

(LYMPHOCYTE OR LYMPHOCYTES)

L8 10 L7 AND (T AND (CELL OR LYMPHOCYTE))

=&gt; duplicate remove L8

PROCESSING COMPLETED FOR L8

L9 10 DUPLICATE REMOVE L8 (0 DUPLICATES REMOVED)

=&gt; d L9 bib abs 1-9

L9 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text	Citing References
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AN 2007:87074 CAPLUS

DN 146:293573

TI Antigenic profiling of glioma **cells** to generate allogeneic vaccines or dendritic **cell**-based therapeutics

AU Zhang, Jian Gang; Eguchi, Junichi; Kruse, Carol A.; Gomez, German G.; Fakhrai, Habib; Schroter, Stephanie; Ma, Wenxue; Hoa, Neil; Minev, Boris; Delgado, Christina; Wepsic, H. Terry; Okada, Hideho; Jadus, Martin R.

CS Diagnostic and Molecular Health Care Group, Veterans Affairs Medical Center, Long Beach, CA, USA

SO Clinical Cancer Research (2007), 13(2, Pt. 1), 566-575

CODEN: CCREF4; ISSN: 1078-0432

PB American Association for Cancer Research

DT Journal

LA English

AB Allogeneic glioma **cell** lines that are partially matched to the patient at class I human leukocyte antigen (**HLA**) loci and that display tumor-assocd. antigens (TAA) or antigenic precursors [tumor antigen precursor proteins (TAPP)] could be used for generating whole tumor **cell** vaccines or, alternatively, for extn. of TAA **peptides** to make autologous dendritic **cell** vaccines. Twenty human glioma **cell** lines were characterized by mol. phenotyping and by flow cytometry for **HLA** class I antigen expression. Twelve of the 20 **cell** lines, as well as analyses of freshly resected glioma tissues, were further characterized for protein and/or mRNA expression of 16 tumor antigen precursor proteins or TAA. These 20 human glioma **cell** lines potentially cover 77%, 85%, and 78% of the U.S. Caucasian population at **HLA**-A, **HLA**-B, and **HLA**-C alleles, resp. All **cells** exhibited multiple TAA expressions. Most glioma **cells** expressed antigen isolated from immunoselected melanoma-2 (Aim-2), B-cyclin, **EphA2**, GP100, {szligbeta}1,6-N-acetylglucosaminyltransferase V (GnT-V), IL13R $\alpha$ 2, Her2/neu, hTert, Mage, Mart-1, Sart-1, and survivin. Real-time PCR technol. showed that glioblastoma specimens

expressed most of the TAA as well. Tumor-infiltrating **lymphocytes** and CD8+ CTL killed T2 **cells** when loaded with specific **HLA-A2+** restricted TAA, or gliomas that were both **HLA-A2+** and also pos. for specific TAA (Mart-1, GP100, Her2/neu, and tyrosinase) but not those **cells** neg. for **HLA-A2** and/or lacking the specific **epitope**. These data provide proof-in-principle for the use of allogeneic, partially **HLA** patient-matched glioma **cells** for vaccine generation or for **peptide** pulsing with allogeneic glioma **cell** exts. of autologous patient dendritic **cells** to induce endogenous CTL in brain tumor patients.

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text	Citing References
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AN 2006:1207176 CAPLUS  
DN 145:504043  
TI Cryptic **peptide epitopes** and their optimized derivatives for vaccination  
IN Kosmatopoulos, Kostantinos  
PA Vaxon Biotech, Fr.  
SO PCT Int. Appl., 49pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 2006120038</u>	A2	20061116	<u>WO 2006-EP5325</u>	20060509
<u>WO 2006120038</u>	A3	20070719		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			

PRAI EP 2005-290984 A 20050509

AB The author discloses the use of optimized derivs. of cryptic native **peptide epitopes** for eliciting an enhanced immune response. In one example, an enhanced cytotoxic **T-cell** response against telomerase was demonstrated in tumor patients receiving initially an optimized **peptide** vaccine followed by vaccination with the native **peptide**.

L9 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text	Citing References
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AN 2006:333546 CAPLUS  
DN 144:329777  
TI **Epitope** variants for enhancing glioma-specific cytotoxic **T cell** response  
IN Storkus, Walter J.; Sato, Hidemitsu; Okada, Hideho; Eguchi, Junichi  
PA University of Pittsburgh of the Commonwealth System of Higher Education, USA

SO PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	<u>WO 2006034334</u>	A2	20060330	<u>WO 2005-US33794</u>	20050921
	<u>WO 2006034334</u>	A3	20060914		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	<u>US 2007167375</u>	A1	20070719	<u>US 2005-231618</u>	20050921
PRAI	<u>US 2004-611797P</u>	P	20040921		

AB The authors disclose **peptide** variants derived from the interleukin-13 receptor  $\alpha 2$ , which exhibit increased affinity for **HLA-A2** and elicit an enhanced cytotoxic **T lymphocyte** (CTL) response. The **peptide** variants can be used as a vaccine for glioma and can be formulated into compns. for medical or veterinary use. In addn., the authors also disclose a **peptide** derived from the **EphA2** tyrosine kinase receptor which may be used for therapy of glioma.

L9 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text	Citing References
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AN 2005:120967 CAPLUS

DN 142:217364

TI Human **EphA2** protein **T cell epitope** agonists for ELISPOT assay and as vaccines against tumor overexpressing **EphA2**

IN Storkus, Walter J.; Kinch, Michael S.

PA University of Pittsburgh-of the Commonwealth System of Higher Education, USA; Medimmune, Inc.

SO PCT Int. Appl., 115 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	<u>WO 2005012350</u>	A2	20050210	<u>WO 2004-US23931</u>	20040722
	<u>WO 2005012350</u>	A3	20050714		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,				

AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

<u>AU 2004261603</u>	A1	20050210	<u>AU 2004-261603</u>	20040722
<u>CA 2533789</u>	A1	20050210	<u>CA 2004-2533789</u>	20040722
<u>US 2005048550</u>	A1	20050303	<u>US 2004-897711</u>	20040722
<u>EP 1651671</u>	A2	20060503	<u>EP 2004-779136</u>	20040722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
<u>JP 2007527225</u>	T	20070927	<u>JP 2006-521960</u>	20040722
<u>US 2006019899</u>	A1	20060126	<u>US 2005-233796</u>	20050923
<u>US 2003-491046P</u>	P	20030730		
<u>US 2004-897711</u>	A1	20040722		
<u>WO 2004-US23931</u>	W	20040722		

**AB EphA2 T-cell epitope** agonists are provided herein. The agonists include **peptides** corresponding to specific fragments of human **EphA2** protein contg. one or more **T-cell epitopes**, and conservative derivs. thereof. The **EphA2 T-cell epitope** agonists are useful in an assay, such as an ELISPOT assay, that may be used to det. and/or quantify a patient's immune responsiveness to **EphA2**. The agonists also are useful in methods of modulating a patient's immune reactivity to **EphA2**, which has substantial utility as a treatment for cancers that overexpress **EphA2**, such as renal **cell carcinoma**. The **EphA2** agonists also can be used to vaccinate a patient against **EphA2**, by in vivo or ex vivo methods.

L9 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text	Citing References
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AN 2005:1201395 CAPLUS  
 DN 144:189389  
 TI **EphA2** as a glioma-associated antigen: A novel target for glioma vaccines  
 AU Hatano, Manabu; Eguchi, Junichi; Tatsumi, Tomohide; Kuwashima, Naruo; Dusak, Jill E.; Kinch, Michel S.; Pollack, Ian F.; Hamilton, Ronald L.; Storkus, Walter J.; Okada, Hideho  
 CS Department of Neurological Surgery, University of Pittsburgh School of Medicine and University of Pittsburgh Cancer Institute, Pittsburgh, PA, 15213, USA  
 SO Neoplasia (Ann Arbor, MI, United States) (2005), 7(8), 717-722  
 CODEN: NEOPFL; ISSN: 1522-8002  
 PB Neoplasia Press Inc.  
 DT Journal  
 LA English  
 AB **EphA2** is a receptor tyrosine kinase and is frequently overexpressed in a wide array of advanced cancers. We demonstrate in the current study that the **EphA2** protein is restrictedly expressed in primary glioblastoma multiforme and anaplastic astrocytoma tissues in comparison to normal brain tissues. To evaluate the possibility of targeting **EphA2** in glioma vaccine strategies, we stimulated human leukocyte antigen (HLA) A2+ peripheral blood mononuclear cells (PBMCs) obtained from healthy donors and glioma patients with autologous dendritic cells (DCs) loaded with synthetic EphA2883-891 **peptide** (TLADFDPRV), which has previously been reported to induce interferon- $\gamma$  in HLA-A2+ PBMCs. Stimulated PBMCs demonstrated antigen-specific cytotoxic **T lymphocyte** (CTL) responses as detected by specific lysis of T2 cells loaded with the EphA2883 **peptide** as well as HLA-A2+ glioma cells, SNB19 and U251, that express **EphA2**. Furthermore, in vivo immunization of HLA-A2

transgenic HHD mice with the EphA2883-891 **peptide** resulted in the development of an **epitope**-specific CTL response in splenocytes, despite the fact that EphA2883-891 is an autoantigen in these mice. Taken together, these data suggest that EphA2883-891 may be an attractive antigen **epitope** for molecularly targeted glioma vaccines.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

**Full Text** **Citing References**

AN 2003:837593 CAPLUS  
DN 139:322275  
TI **Peptide T epitopes** of the **EphA2** antigen for antitumor immunotherapy  
IN Kosmatopoulos, Kostas; Alves, Pedro  
PA Institut National de la Sante et de la Recherche Medicale INSERM, Fr.;  
Institut Gustave Roussy  
SO Fr. Demande, 22 pp.  
CODEN: FRXXBL  
DT Patent  
LA French  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>PI</u>	<u>FR 2838742</u>	A1	20031024	<u>FR 2002-5048</u>	20020423
	<u>FR 2838742</u>	B1	20040709		
	<u>CA 2482930</u>	A1	20031106	<u>CA 2003-2482930</u>	20030423
	<u>WO 2003091383</u>	A2	20031106	<u>WO 2003-FR1280</u>	20030423
	<u>WO 2003091383</u>	A3	20040401		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	<u>AU 2003262810</u>	A1	20031110	<u>AU 2003-262810</u>	20030423
	<u>EP 1497417</u>	A2	20050119	<u>EP 2003-740654</u>	20030423
	<u>EP 1497417</u>	B1	20070314		
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
	<u>AT 356867</u>	T	20070415	<u>AT 2003-740654</u>	20030423
	<u>US 2006034856</u>	A1	20060216	<u>US 2005-511273</u>	20050627
<u>PRAI</u>	<u>FR 2002-5048</u>	A	20020423		
	<u>WO 2003-FR1280</u>	W	20030423		

AB The invention discloses **peptides** constituting **EphA2** antigen **T epitopes**, presented by MHC I. The **peptides** are useful in particular for antitumor immunotherapy.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

**Full Text** **Citing References**



AN 2003:982383 CAPLUS  
 DN 140:75821  
 TI **EphA2 as Target of Anticancer Immunotherapy: Identification of HLA-A\*0201-Restricted Epitopes**  
 AU Alves, Pedro M. S.; Faure, Olivier; Graff-Dubois, Stephanie; Gross, David-Alexandre; Cornet, Sebastien; Chouaib, Salem; Miconnet, Isabelle; Lemonnier, Francois A.; Kosmatopoulos, Kostas  
 CS INSERM487, Institut Gustave Roussy, Villejuif, Fr.  
 SO Cancer Research (2003), 63(23), 8476-8480  
 CODEN: CNREA8; ISSN: 0008-5472  
 PB American Association for Cancer Research  
 DT Journal  
 LA English  
 AB **EphA2 (Eck)** is a tyrosine kinase receptor that is overexpressed in several human cancers such as breast, colon, lung, prostate, gastric carcinoma, and metastatic melanoma but not in nonmalignant counterparts. To validate **EphA2** as a tumor antigen recognized by CD8+ T lymphocytes, we used reverse immunol. approach to identify HLA-A\*0201-restricted epitopes. Peptides bearing the HLA-A\*0201-specific anchor motifs were analyzed for their capacity to bind and stabilize the HLA-A\*0201 mols. Two peptides, EphA258 and EphA2550, with a high affinity for HLA-A\*0201 were selected. Both peptides were immunogenic in the HLA-A\*0201-transgenic HHD mice. Interestingly, peptide-specific murine CTLs cell lines responded to COS-7 cells coexpressing HLA-A\*0201 and EphA2 and to EphA2-pos. human tumor cells of various origin (renal cell, lung, and colon carcinoma and sarcoma). This demonstrates that EphA258 and EphA2550 are naturally processed from endogenous EphA2. In addn., EphA258 and EphA2550 stimulated specific CD8+ T cells from healthy donor peripheral blood mononuclear cells. These T cells recognized EphA2-pos. human tumor cells in an HLA-A\*0201-restricted manner. Interestingly, EphA2-specific CD8+ T cells were detected in the peripheral blood mononuclear cells of prostate cancer patients. These results show for the first time that EphA2 is a tumor rejection antigen and lead us to propose EphA258 and EphA2550 peptides for a broad-spectrum-tumor immunotherapy.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text	Citing References
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AN 2003:613807 CAPLUS  
 DN 139:275676  
 TI Disease Stage Variation in CD4+ and CD8+ T-Cell Reactivity to the Receptor Tyrosine Kinase **EphA2** in Patients with Renal Cell Carcinoma  
 AU Tatsumi, Tomohide; Herrem, Christopher J.; Olson, Walter C.; Finke, James H.; Bukowski, Ronald M.; Kinch, Michael S.; Ranieri, Elena; Storkus, Walter J.  
 CS Departments of Surgery and Immunology, University of Pittsburgh School of Medicine, Pittsburgh, PA, 15213, USA  
 SO Cancer Research (2003), 63(15), 4481-4489  
 CODEN: CNREA8; ISSN: 0008-5472  
 PB American Association for Cancer Research  
 DT Journal  
 LA English  
 AB The authors have evaluated CD8+ and CD4+ T-cell responses against a

new tumor-assocd. antigen, the receptor tyrosine kinase **EphA2**, which is broadly expressed in diverse cancer histologies and is frequently overexpressed in advanced stage/metastatic disease. They report herein that **EphA2** is overexpressed in renal **cell** carcinoma (RCC) **cell** lines and clin. specimens of RCC, and find that the highest levels of **EphA2** are consistently found in the most advanced stages of the disease. The authors identified and synthesized 5 putative **HLA** class I-binding and 3 class II-binding **peptides** derived from **EphA2** that might serve as targets for immune reactivity. Each **peptide** induced specific, tumor-reactive CD8+ or CD4+**T-cell** responses as measured using IFN- $\gamma$  enzyme-linked immunospot assays. The **EphA2 peptides** elicited relatively weak responses from CD8+ **T cells** derived from normal healthy volunteers or from RCC patients with active disease. In marked contrast, immune reactivity to **EphA2**-derived **epitopes** was greatly enhanced in CD8+ **T cells** that had been isolated from patients who were rendered disease-free, after surgery. Furthermore, enzyme-linked immunospot analyses demonstrated prominent **EphA2**-restricted T-helper 1-type CD4+ **T cell** activity in patients with early stage disease, whereas T-helper 2-type and T regulatory-type responses predominated in patients with more advanced forms of RCC. Thus, the immune system of cancer patients actively monitors **EphA2**-derived **epitopes**, and the magnitude and character of **T-cell** responses to **EphA2 epitopes** may convey much-needed predictive information about disease stage and outcome.

RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text Citing References

AN 2002:937303 CAPLUS

DN 138:20443

TI Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes

IN Kondo, Akihiro; Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto, Yoshimasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunoshin

PA Takara Bio Inc., Japan

SO Jpn. Kokai Tokkyo Koho, 386 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	<u>JP 2002355079</u>	A	20021210	<u>JP 2002-69354</u>	20020313
PRAI	<u>JP 2001-73183</u>	A	20010314		
	<u>JP 2001-74993</u>	A	20010315		
	<u>JP 2001-102519</u>	A	20010330		

AB A method and kit for detecting endocrine-disrupting chems. using DNA microarrays are claimed. The method comprises prep. a nucleic acid sample contg. mRNAs or cDNAs originating in **cells**, tissues, or organisms which have been brought into contact with a sample contg. the endocrine disruptor. The nucleic acid sample is hybridized with DNA microarrays having genes affected by the endocrine disruptor or DNA fragments originating in these genes have been fixed. The results obtained are then compared with the results obtained with the control sample to select the gene affected by the endocrine disruptor. Genes whose expression is altered by tri-Bu tin, 4-octaphenol, 4-nonylphenol, di-N-Bu phthalate,

dichlorohexyl phthalate, octachlorostyrene, benzophenone, diethylhexyl phthalate, diethylstilbestrol (DES), and 17- $\beta$  estradiol (E2), were found in mice by DNA chip anal.

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